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Identification of linear B-cell epitopes in the capsid, NS4a and domain III region in the E glycoprotein of yellow fever virus

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Background: Yellow fever virus (YFV) is a mosquito-borne virus that causes viral hemorrhagic fever in tropical parts of both Africa and South America. The virus has re-emerged and has become a public health concern across the world, despite the availability of a highly efficacious vaccine. This vaccine cannot be administered to immune-compromised individuals, thus the identification and mapping of viral epitopes is important for development of subunit vaccines and improved diagnostics. Our aim was to identify linear B-cell epitopes on the capsid, NS4a and domain III region of the envelope (EDIII) glycoprotein of YFV using overlapping peptide libraries.

Methods & Materials: Putative hydrophobic and hydrophilic regions along the length of each protein were predicted using BepiPred and ABCpred prediction software. Surface accessibility and antigenicity were done using the Immune Epitope Database (IEDB) version 2.0 software (www.ImmuneEpitope.org). Bioinformatics was used to identify 28 overlapping peptides (8 mer length offset by 3) representing predicted epitopic regions on the capsid protein, NS4a protein and EDIII protein. Using an in-house ELISA, the peptides were screened for reactivity using immune sera from 12 patients with a history of vaccination against YFV.

Results: Overlapping peptides covering the region IPSSASPWSWPDLDLKPGAA of NS4a protein reacted with 6/12 patient sera. Overlapping peptides covering the region KTKQIGNRPGPSRGVQG of capsid protein reacted with 4/12 patient sera. Overlapping peptides 10-28 of EDIII reacted with 4/12 patient sera. Peptides 14, 15, 22, 23 and 28 of EDIII showed consistent reactivity against all the patient sera. Overlapping peptides 22 and 23 showed higher reactivity compared to the other peptides.

Conclusion: Prediction software was used to identify epitopic regions based on predicted amino acid sequences. Only a proportion of sera from vaccinated individuals reacted against peptides from the NS4a and capsid proteins. In comparison 12/12 sera reacted against five peptides based on the sequence from the EDIII protein suggesting these regions were more likely significant epitopic regions. Epitopic regions identified using prediction software require biological assays for confirmation. Further studies to determine their role in protective immunity would indicate their usefulness in vaccine development.

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What happens with rabies disease after successive inoculations of rabies virus from different genetic lineages?

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Background: Rabies is a neurological zoonosis causing a lethal infection in all mammalians, including humans. The etiological agent of the illness is the rabies virus (RABV) that belong to the genus Lyssavirus, family Rhabdoviridae. According to the World Health Organization rabies is a neglected disease causing about 60.000 deaths people by year worldwide mainly in Africa and Asia. Rabies could be maintained by aerial and terrestrial cycles, the aerial cycle has bats as the main reservoir and in most developing countries dogs represent the major rabies reservoir in terrestrial cycle. The RABV is a RNA virus and differences in genome of the virus could be identified according to the reservoir.

Methods & Materials: This work was made to understand the influence in pathogenesis of rabies disease of the differences in the genome of RABV. To answer this question, three samples of RABV isolated from different reservoirs (dog, haematophagous bat and non haematophagous bat) with different genetic lineages were selected. After that each one of the samples was submitted to ten successive inoculations in mice by intracerebral route. The group of mice was formed by six animals that received food and water *at libidum*. The animals were monitored daily and the development of clinical signs and the date of death were recovered.

Results: The rabies had a variable incubation period between 3 to 5 days in the inoculated mice, the clinical course of the infection was 4 days and all mice experimentally infected with RABV developed neurological signs as apathy, ataxia, muscle spasms paralysis and death.

Conclusion: Our work shown the RABV maintained highly pathogenic and ten successive inoculations of the virus were not suitable to attenuate the virus. These findings highlight the importance of the understanding pathogenesis of RABV and its value as an aid to support rabies surveillance.

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